UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,821	08/17/2001	Katherine D. Gordon	1540/140	4514

2101 7590 09/24/2003

BROMBERG & SUNSTEIN LLP
125 SUMMER STREET
BOSTON, MA 02110-1618

EXAMINER	
BAHAR, MOJDEH	

ART UNIT	PAPER NUMBER
1617	16

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/932,821	Applicant(s) GORDON ET AL.	
	Examiner Mojdeh Bahar	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-3 (in part), 7-11 (in part), 4, 12-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3(in part), 7-11 (in part) 5-6, 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and response to the office action of December 17, 2002, filed June 20, 2003 are acknowledged.

Claims 1-3 (in part), 5-6, 7-11 (in part) and 22-25 are herein examined on the merits in so far as they read on the elected species.

This application contains claims 4, 12-21 as well as claims 1-3 (in part) and 7-11 (in part) drawn to an invention nonelected with traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (limiting the scope of claims 1-3 and 7-11 to the elected invention) (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 (in part), 5-6, 7-11 (in part) and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bechgaard et al. (USPN 5,397,771) in view of PDR (Valium brand of diazepam injection) page 2676-78 and Steppuhn et al. (5,385,903).

Bechgaard et al. (USPN 5,397,771) teaches a method of administering a composition comprising benzodiazepines, and more specifically diazepam (an anti-epileptic compound), vegetable oil (i.e., soybean oil, peanut oil, corn oil, olive oil, sunflower oil, castor oil), see specifically col. 4, lines 30-32, col. 10, lines 64-67 and claims 1, 12 and 13. Bechgaard et al. (USPN 5,397,771) also teaches that its pharmaceutical composition may also include alcohols, such as benzyl alcohol, see specifically Table 7 as well as col. 10, lines 50-63. Bechgaard et al. (USPN 5,397,771) further teaches that its vehicle system increases the possibility for designing a controlled release formulation such as diazepam formulation which avoids peak plasma concentrations, see col. 10, lines 42-49, see also Tables 1-5 which show that the peak plasma concentrations after administration of benzodiazepines is reaches in less than 4 hours. Bechgaard teaches intranasal and intravenous administration of its composition, see abstract and example 7. Bechgaard also teaches that the delivery system can be optimized, see particularly col. 10, lines 21-23.

Bechgaard et al. (USPN 5,397,771) does not particularly teach the administration of its diazepam composition in the form of an injection.

PDR teaches a composition comprising diazepam and benzyl alcohol employed in a method of treating seizures. PDR further teaches that diazepam is not water soluble. PDR further teaches that the composition is administered intramuscularly and intravenously.

Steppuhn et al. (5,385,903) teaches that diazepam in sesame oil can be administered subcutaneously, see col. 2, lines 28-67.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the composition of Bechgaard in the form of an injection.

One of ordinary skill in the art would have been motivated to administer the composition of Bechgaard subcutaneously because intraconversion of dosage forms and routes of administration are within the skill of the artisan and are therefore obvious. Furthermore, diazepam is known to be administered in injection formulations, e.g., intravenous, intramuscularly, and subcutaneously.

Response to Arguments

Applicant's arguments filed June 20, 2003 have been fully considered but they are not persuasive.

Applicant argues that the route of administration taught in Bechgaard et al. is different than that disclosed by applicant and that there would be no motivation to change the route of administration of Bechgaard et al. Note that intraconversion of dosage forms and routes of administration are within the purview of the Skilled Artisan and are therefore obvious, absent evidence to the contrary. No such evidence is seen. More importantly, please not that Bechgaard et al. does indeed teach other routes of administration, e.g., and intravenous route. Applicant argues against Examiner's statement that the intraconversion of dosage forms is within the purview of the Skilled Artisan stating that it was "apparently not obvious to Bechgaard et al. to change the route of administration from intravenous to nasal form." Note that this statement does not correctly reflect the teachings of Bechgaard et al. because examples 7 and 13 in

Bechgaard refers to both intravenous and nasal administration. Furthermore in column 22. Bechgaard teaches that absorption of intranasal diazepam is very similar to its intravenous injection, see col. 22, lines 61-65.

Applicant then argues that Bechgaard requires n-glycofurol and the instant claims do not require this component. Note that n-glycofurol, is a widely known pharmaceutical solvent. Note that the mere addition or subtraction of a pharmaceutical necessity (i.e., excipient) does not render a known composition unobvious. The addition/subtraction of pharmaceutical excipients are within the purview of the Skilled artisan and are therefore obvious, absent evidence to the contrary. No such evidence is seen.

Applicant argues that the Skilled artisan would have no expectation of success, "because the entire novelty and non-obviousness of Bechgaard et al. lies in the surprising results seen with rapid peak plasma concentrations when the route of administration is nasal/mucosal and NOT intravenous or anything else." Note that applicant's characterization of the prior art is factually flawed since Bechgaard explicitly states:

> "Surprisingly it has been found that the intranasal absorption of e.g., benzodiazepines, such as clonazepam and diazepam, in the vehicles according to the invention is very similar to intravenous injection," col. 22, lines 61-65.

Applicant then argues that the route of administration taught in Bechgaard et al. is different than that disclosed by applicant and that there would be no motivation to change the route of administration of Bechgaard et al. Note that intraconversion of dosage forms and routes of administration are within the purview of the Skilled Artisan and are therefore obvious, absent evidence to the contrary. No such evidence is seen.

Applicant argues that there is nomotivation to combine Bechgaard with other references because Bechgaard teaches away from employment of needles, i.e., injectable formulations. Note that as cited above Bechgaard explicitly teaches intravenous formulations, see for examples 7 and 13.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
September 17, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER
9/22/03